Abstracts

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Factors affecting symptomatic vs asymptomatic vein graft stenoses in lower extremity bypass grafts

Landry GJ, Liem TK, Mitchell EL, et al. Arch Surg 2007;142:848-54.

Conclusions: Symptomatic vein graft stenosis is associated with the presence of distal vein graft lesions, alternative conduit grafts, and larger decreases in the ankle-brachial index (ABI). Graft patency after graft revision is not affected by whether the vein graft stenosis was or was not associated with symptoms.

Summary: Stenosis of lower extremity vein grafts is often asymptomatic. This study was undertaken to characterize symptomatic vs asymptomatic vein grafts and to determine if the presence of symptoms influenced subsequent patency of vein grafts after revision. This was a retrospective analysis of a prospectively maintained database from a combined University and Department of Veterans Affairs Vascular Surgical Service. There were 219 lower extremity vein graft revisions performed in 161 patients between January 1995 and January 2007. Patients with vein graft stenoses were considered symptomatic if they had recurrence of the symptoms that had prompted the original placement of the vein graft. Both univariate and multivariate analysis were used to develop a model of independent predictors of symptomatic recurrence. Patency rates for symptomatic and asymptomatic stenotic vein grafts were compared after revision.

There were 125 asymptomatic and 94 symptomatic vein graft lesions revised. Lesions associated with symptoms had a significantly greater drop in ABI than asymptomatic lesions (0.21 ± 0.03 vs 0.18 ± 0.02, $P = .003$). Vein graft stenoses that were located in the distal graft or in the outflow artery were also more likely to be associated with symptom recurrence ($P = .048$). By multivariate analysis, a decrease in ABI (odds ratio, 6.803; 95% confidence interval [CI], 1.418-32.258; $P = .02$) and use of alternative vein conduits (odds ratio. 2.633; 95% CI, 1.243-5.578; $P = .01$) were independent predictors of symptomatic vein graft stenosis. There were also strong trends towards symptomatic recurrence being associated with other systemic manifestations of atherosclerosis such as cerebrovascular disease or coronary artery disease ($P = .06$). Patients with diabetes or renal failure and current smokers were not more likely to present with recurrent symptoms. Symptomatic stenoses were more frequent in revisions performed between 1 and 2 years postoperatively (56%) than in the first year after the operation (37%, $P = .003$). Assisted primary patency rates of grafts revised with symptomatic vs asymptomatic stenoses were not different (82% symptomatic and 88% asymptomatic at 5 years; $P = .30$).

Comment: The article defines, for the first time, factors associated with symptomatic vein graft stenoses. Unfortunately, although stenoses revised in alternative conduit grafts and stenoses revised >1 year after graft implantation are more frequently associated with symptoms, a significant number of patients in those groups also have asymptomatic graft stenosis of sufficient severity that the graft requires revision. At this time, a life-long policy of periodic surveillance of lower extremity vein grafts with duplex scanning still seems prudent.

Shifting paradigms in the treatment of lower extremity vascular disease: A report of 1000 percutaneous interventions

DeRubertis BG, Faries PL, McKinsey JF, et al. Ann Surg 2007;246:415-424.

Conclusion: The first-line therapy for patients with chronic lower extremity ischemia should be a percutaneous intervention.

Summary: The authors report retrospective analysis of 1000 percutaneous infrainguinal interventions. Claudication was the indication for intervention in 46.3%, and limb-threatening ischemia was the indication in 52.7% (rest pain, 27.7%; tissue loss, 72.3%). Patients were treated with a variety of catheter-based techniques, including angioplasty, angioplasty and stenting, laser angioplasty, and atherectomy. Femoral, popliteal, and tibial vessels were treated. Men comprised 57.3% of patients, 58% of patients had diabetes, and chronic renal insufficiency was present in 39%. The 30-day mortality rate was 0.5%. In patients with claudication, 2-year primary and secondary patency rates were 62.4% and 79.3%. At 2 years, only 0.5% of claudicant patients had undergone amputations. In patients with limb-threatening ischemia, rates for 2-year primary patency, secondary patency, and limb salvage were 37.4%, 55.4%, and 79.3%, respectively. Predictors of recurrent disease included limb threat as the indication for intervention ($P < .0001$), hypercholesterolemia ($P = .001$), diabetes ($P = .003$), coronary artery disease ($P = .047$), and TransAtlantic Inter-Society Consensus (TASC) D lesions ($P = .050$). Of the patients with recurrent disease, 60.3% underwent a successful percutaneous reintervention, 7.5% required no further intervention, 11.7% underwent bypass, and 20.5% had amputation.

Comment: This is a retrospective analysis of a large number of patients treated for evolving indications with continually changing technology. The results are not surprising, and the predictors of failure not unexpected. Unfortunately, this lesion-based analysis is out dated. The authors also did not tell us about those who were medically managed, those treated with open operations, the nature of the wounds in the patients with critical limb ischemia, and who underwent primary amputation. There was no quality of life evaluation in those treated. Compared with most open series of infrainguinal revascularization, a high percentage of the patients had claudication. Overall, the article tells us what a group of surgeons with seemingly relatively liberal indications for intervention and favoring catheter-based techniques *did*. It also tells us a bit about how the intervention worked out. It doesn't really tell patients how it will work out for them, nor does it tell surgeons what they *should* do.

Effect of statin withdrawal on frequency of cardiac events after vascular surgery

Schouten O, Hoeks SE, Welten GM, et al. Am J Cardiol 2007;1000: 316-20.

Conclusion: Statin withdrawal in the perioperative period after vascular surgery is associated with increase risks of perioperative adverse cardiac events.

Summary: The incidence of adverse cardiac events increases in patients with acute coronary syndrome who have withdrawal of their statin medication (J Cardiothorac Anesthes 2003;17:90-100). There are no intravenous formulas for statins, thus interruption of statins in the postoperative period occurs frequently, especially in patients with postoperative ileus. In this study, the authors studied 298 consecutive patients who underwent major vascular surgery and who were also taking a statin medication. The goal of the study was to assess the effect of postoperative cardiac outcome after perioperative statin withdrawal.

Patients were evaluated with detailed cardiac history and determination of medication use, including the particular type of statin each patient was taking. Troponin levels were measured on postoperative days 1, 3, and 7, and 30. Troponin levels were also obtained whenever indicated clinically by electrocardiographic changes. End points of the study were myocardial infarction, postoperative troponin release, and a combination of cardiovascular death and nonfatal myocardial infarction. Cox proportional hazard analysis and multivariant analysis were used to assess the influence of statin type and the effect of discontinuation of statins on occurrence of study end points.

Perioperative discontinuation of statin medication was associated with an increased risk of troponin release (hazard ratio [HR], 4.6; 95% confidence interval [CI], 2.2-9.6). Statin discontinuation was also associated with an increased risk of the combination of cardiovascular death and myocardial infarction (HR, 7.5; 95% CI, 2.8-10.1). Fluvastatin, an extended-release statin, was associated with fewer perioperative events compared with pravastatin, simvastatin, and atorvastatin.

Comment: Evidence is accumulating that statin withdrawal in the perioperative period is harmful for vascular surgical patients. Obviously, this is not due to perioperative changes in lipid levels but likely involves some of the pleiotropic effects of statins, such as inhibition of inflammation, antithrombotic effects, and modulation of endothelial function. Pleiotropic effects are present within hours of statin administration. Such effects can be rapidly lost with acute withdrawal of a statin medication. Whenever possible, vascular surgical patients should be started on statins preoperatively and maintained on statins during their perioperative period.

TGF-Beta and CTGF-Mediated Fibroblast Recruitment Influences Early Outward Vein Graft Remodeling

Jiang Z, Yu P, Tao M, et al. Am J Physiol Heart Circulatory Physiol 2007; 293: H482-H488.

Conclusions: Elevated wall shear stress increases production of tissue growth factor-β (TGF-β) and connective tissue growth factor (CTGF) leading to increased differentiation of fibroblasts to myofibroblasts. Levels of TGF-β and CTGF correlate inversely with outward remodeling of the vein graft wall.

Summary: Placement of a venous conduit into an arterial system leads to acute alterations in shear stress in the vein graft wall. Shear influences both the morphology of the graft wall and intramural growth. Increased wall shear promotes luminal expansion, and elevated circumferential wall stress leads to wall thickening and stabilization of luminal diameter. Both TGF-β and CTGF regulate adventitial remodeling. The authors postulate increased

levels of CTGF and TGF-β will induce recruitment of myofibroblasts and provoke adventitial reorganization to limit outward remodeling of the vein graft in response to increased intramural wall stress.

The authors created a model using a distal arterial venous fistula in the neck of rabbits that results in circumferential wall shear stress. Neck and fistula veins were harvested at 1, 3, and 7 days after implantation. Flow rates were recorded at the time of graft implantation and harvest using an ultrasonic flow meter. Real-time polymerase chain reaction and enzyme-linked immunosorbent assays were used to assess production of CTGF and TGF-β_1.

With this model, the authors demonstrated increased production of TGF-β and CTGF in response to elevated wall stress. TGF-β and CTGF increased expression correlated with enhanced differentiation from fibroblasts to myofibroblasts, as reflected in increases in the α-actin–positive cells in the adventitia. Levels of α-actin, TGF-β, and CTGF were all inversely correlated with outward remodeling of the graft wall.

Comment: Wolinsky and Glagov originally demonstrated arterial adaption to maintain lumen diameter in atherosclerotic arteries. In vein grafts, this adaptive response might be limited by TGF-β and CTGF increases in myofibroblasts. Such an adaption may maintain vein wall integrity in the face of increased intraluminal pressure but may ultimately prove disadvantageous because it may limit the ability of the vein graft to maintain luminal diameter in response to the development of intimal hyperplasia.

Temporary worsening of renal function after aortic surgery is associated with higher long-term mortality

Welten GM, Schouten O, Chonchol M, et al. Am J Kidney Dis 2007;50: 219-28.

Conclusion: Temporary worsening of renal function after open surgery for abdominal aortic aneurysm (AAA) is associated with an increased long-term mortality rate.

Summary: The authors sought to determine the effects of temporary renal dysfunction on the long-term mortality rate in patients undergoing AAA surgery. From January 1995 to June 2006, 1324 patients underwent elective open AAA repair in a single center in Rotterdam. Creatinine clearance was measured preoperatively and on postoperative days 1, 2, and 3. The patients were then divided into three groups. Group 1 had improved or unchanged renal function. Group 2 had temporary worsening of renal function with a >10% decrease on day 1 or 2, and then recovery ≤10% of baseline by day 3. Group 3 patients had persistent worsening of renal function as defined by a >10% decrease in creatinine clearance compared with the baseline value.

The 30-day mortality rates in groups 1, 2, and 3 were 1.2%, 5%, and 12.6%, respectively. Adjusting for postoperative complications and baseline characteristics, the 30-day mortality rate was greatest in the patients with persistent worsening of renal function (hazard ratio (HR), 7.3; 95% confidence interval [CI], 2.7-19.8). Those who had temporary worsening of renal function also had an increased mortality risk (HR, 3.7; 95% CI, 1.4-9.9). Follow-up was for 6.0 ± 3.4 years. During follow-up, 348 patients (36.5%) died. The HR for late death was 1.7 (95% CI, 1.3-2.3) in the patients who had persistent worsening of renal function. For those who had temporary worsening of renal function, the HR for death was 1.5 (95% CI, 1.2-1.4). There was a significant association between perioperative blood loss and worsening of renal function ($P < .001$) and between length of suprarenal aortic clamping and worsening of renal function ($P < .001$). There was also a greater incidence of hypertension in the patients with temporary and persisting renal dysfunction ($P < .001$).

Comment: Another recent study suggested minimal changes in renal function after cardiothoracic surgery had little impact on long-term prognosis (J Am Soc Nephrol 2004;15:1597-605). The current study reaches an opposite conclusion. Although this study was retrospective, the mean follow-up was long (6 years) and the number of patients was large (n = 1324). It is reasonable, therefore, to conclude that any significant worsening of perioperative renal function in an AAA patient carries an adverse prognosis both in the near- and long-term. Although it seems nice when transient renal dysfunction after AAA surgery returns to baseline levels, it doesn't appear to do the patient any good.

Effects of random allocation to vitamin E supplementation on the occurrence of venous thromboembolism: Report from the Women's Health Study

Glynn RJ, Ridker PM, Goldhaber SZ, et al. Circulation 2007;116:1497-503.

Conclusion: Vitamin E supplementation lowers the risk of venous thromboembolism (VTE).

Summary: Vitamin E supplementation may serve as a natural antagonist of vitamin K in healthy adults. Whether vitamin E can sufficiently antagonize vitamin K activity to decrease the risk of VTE is unknown. The Women's Health Study tested the effects of vitamin E supplementation for 10 years on the risk of cardiovascular disease or cancer in a large group of women without these diseases at study entry. The study randomized 39,876 women aged ≥45 years to receive 600 IU of vitamin E, or placebo, on alternate days. Before randomization, blood samples were obtained from 26,779 participants to determine G20210A prothrombin gene mutation, factor V Leiden, and 5,10 methylenetetrahydrofolate reductase (MTHFR) gene polymorphisms. The authors evaluated development of unprovoked VTE (no known diagnosis of cancer and no recent surgery or trauma).

During a median follow-up of 10.2 years, VTE developed in 482 women, 213 in the vitamin E group and 269 in the placebo group, a 21% hazard reduction in the vitamin E group (relative hazard, 0.79; 95% confidence interval [CI], 0.66-0.94; $P = .010$). For unprovoked VTE, the hazard reduction was 27% (relative hazard, 0.73; 95% CI, 0.57-0.94; $P = .016$). A subgroup analysis of the 3% of women in the study who reported VTE before randomization found they had a 44% hazard reduction (relative hazard, 0.56; 95% CI, 0.31-1.00; $P = .048$) with vitamin E supplementation. Women without prior VTE had an 18% hazard reduction (relative hazard, 0.82; 95% CI, 0.68-0.99; $P = .040$). In women with either the prothrombin gene mutation or factor V Leiden, the hazard reduction was 49% with vitamin E treatment (relative hazard, 0.51; 95% CI, 0.30-0.87; $P = .014$).

Comment: The Women's Health Study itself, and many recent meta-analysis, have not supported a recommendation for vitamin E supplementation to reduce overall cardiovascular events (JAMA 2005;295:56-65 and Lancet 2003;361:2017-2023). The finding that vitamin E supplementation may prevent VTE is, however, not at odds with these previous observations. Arterial and venous events may not share similar mechanisms in all cases. Given the size of this study and its prospective nature, it does appear vitamin E may lower the risk of VTE, especially in woman with genetic risk factors.

Seasonal variation in surgical outcomes as measured by the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP)

Englesbe MJ, Pelletier SJ, Magee JC, et al. Ann Surg 2007;246:456-65.

Conclusion: There are seasonal variations in surgical outcomes with respect to postoperative morbidity and mortality.

Summary: The complete experience of a surgical procedure is complex and involves interactions between both systems and individuals. It is assumed that increased surgeon experience can help produce favorable outcomes. In July and August, there are relatively new trainees in most academic medical centers. At this time of the year, the trainees are less familiar with their roles and responsibilities. It is postulated there may be more adverse outcomes in surgical procedures performed early in the academic year vs later. The authors propose that the National Surgical Quality Improvement Program (NSQIP) is a database that is sufficiently large to allow a multicenter, risk-adjustment analysis of surgical morbidity and mortality on a month-to-month basis. In this study, the authors use 30-day morbidity and mortality rates derived from NSQIP-participating hospitals and compared two periods of care: an early group from July 1 to August 30 and a late group from April 15 to June 15. The postoperative morbidity rate was 18% higher in the early (n = 9941) vs late (n = 10, 310) groups (odds ratio, 1.18; 95% confidence interval [CI], 1.07-1.29, $P = .0005$; c-index, 0.794). Mortality was 41% higher in the early group compared with the late group (odds ratio, 1.41; 95% CI, 1.11-1.80; $P = .005$; c-index 0.938).

Comment: The study really cannot reliably implicate inexperience of resident trainees as contributing to the so-called July effect. No hospitals without training programs were included as controls. In addition, other studies have suggested a "July effect" does not exist (Surgery 2001;130: 346-53 and J Gen Intern Med 2003;18:639-45). The authors also noted an uptake in morbidity and mortality in December. At this point, resident inexperience is not likely important. Also, many attending surgeons take a vacation in July and August; therefore, slightly more urgent cases may be performed in those months than at other times of the year. It may be that less attending supervision in peak vacation months or more urgent surgery in the summer months and December are contributing more to seasonal variation in surgical morbidity and mortality than the inexperience of resident physicians.

The female advantage in cardiovascular disease: Do vascular beds contribute equally?

Kardys I, Vliegenthart R, Oudkerk M, et al. Am J Epidemiol 2007;166: 403-12.

Conclusion: There is a larger gender difference in atherosclerosis of the coronary vessels than in other vascular beds, with women having less severe disease than men. There are no gender differences in the aorta and lower extremity vessels.

Summary: It is widely acknowledged that women have less incidence of coronary heart disease than men. In this study, the authors sought to characterize gender differences in cardiovascular disease according to vascular site. Degrees of coronary, carotid, peripheral, and aortic atherosclerosis were compared in men and women aged >55 years from the population-based Rotterdam Study. The study used data collected between 1997 and